

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1654	gray-j\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L2	747	mulligan-\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L3	45565	lee-j\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L4	40807	lee-s\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L5	86667	1 or 2 or (3 or 4)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L6	2	1 and 2 and (3 or 4)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L7	3939	codon with optimiz\$4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:41
L8	52	7 with (gagpol or gag or pol)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L9	1	5 and 8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L10	37	5 and 7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L11	3	1 and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:43
L12	2791	("Children's" with Medical with Center).as. or (Harvard).as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44

L13	16	12 and 5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44
L14	0	7 and 13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44
L15	14	13 not (6 or 11)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44
L16	44	(hiv or lentivir\$4 or maloney or vecisular) with (codon-optimiz\$6 or (codon adj2 optimiz\$6))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L17	65	(hiv or lentivir\$4 or maloney or vecisular) same (codon-optimiz\$6 or (codon adj2 optimiz\$6))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L18	624	(hiv or lentivir\$4 or maloney or vecisular) and (codon-optimiz\$6 or (codon adj2 optimiz\$6))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L19	30	((hiv or lentivir\$4 or maloney or vecisular) same (codon-optimiz\$6 or (codon adj2 optimiz\$6))) not ((gag or pol) with (codon-optimiz\$6 or (codon adj2 optimiz\$6)))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L20	85	biomedica-\$.as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:46
L21	53	mitrophanous-\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:46
L22	4	kotsopoulou-\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:46
L23	114	kingsman-a\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:47
L24	165	kingsman-\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:47

L25	125	kingsman-s\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:47
L26	74	23 and 25	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L27	153	(Oxford with biomedica).as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L28	238	20 or 27	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L29	2961	kim-n\$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L30	3121	21 or 22 or 23 or 24 or 25 or 29	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:49
L31	2	21 and 22 and 24 and 29	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:51
L32	6	30 and 8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:55
L33	1290	"RRE" or (rev adj3 response adj3 element\$1) or "RREs"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:58
L34	8156	"CTEs" or "CTE" or (constitutive with transport with element\$1)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:56
L35	9370	33 or 34	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:56
L36	504	35 with (devoid or lack\$4 or deficient or without)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:57



L37	14	30 and 36	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:58
L38	1	5 and 36	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:58
L39	14	37 and (lentivir\$4 or retrovir\$4 or HIV or (human adj2 immunodeficiency adj2 vir\$4))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:06
L40	6	39 and 7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:01
L41	5	39 and 8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:59
L42	8	39 not 40	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:04
L43	3	"6669936".pn. or "6312682".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:04
L44	104	36 and (lentivir\$4 or retrovir\$4 or HIV or (human adj2 immunodeficiency adj2 vir\$4))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:06
L45	7	36 and (lentivir\$4 or retrovir\$4 or HIV or (human adj2 immunodeficiency adj2 vir\$4)) and 18	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:07

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1636GXL

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks  
(ROSPATENT) added to list of core patent offices covered  
NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status  
data from INPADOC  
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available  
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded  
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN  
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced  
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
NEWS 10 MAR 22 KOREAPAT now updated monthly; patent information enhanced  
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY  
NEWS 12 MAR 22 PATDPASPC - New patent database available  
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags  
NEWS 14 APR 04 EPFULL enhanced with additional patent information and new  
fields  
NEWS 15 APR 04 EMBASE - Database reloaded and enhanced  
NEWS 16 APR 18 New CAS Information Use Policies available online  
  
NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that  
specific topic.

All use of STN is subject to the provisions of the STN Customer  
agreement. Please note that this agreement limits use to scientific  
research. Use for software development or design or implementation  
of commercial gateways or other similar uses is prohibited and may  
result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005

=> FILE MEDLINE EMBASE BIOSIS CAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 15:35:52 ON 21 APR 2005

FILE 'EMBASE' ENTERED AT 15:35:52 ON 21 APR 2005  
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 15:35:52 ON 21 APR 2005  
Copyright (c) 2005 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> S (GRAY, ?)/IN,AU  
'IN' IS NOT A VALID FIELD CODE  
'IN' IS NOT A VALID FIELD CODE  
L1 63641 (GRAY, ?)/IN,AU

=> S (MULLIGAN, ?)/IN,AU  
'IN' IS NOT A VALID FIELD CODE  
'IN' IS NOT A VALID FIELD CODE  
L2 6393 (MULLIGAN, ?)/IN,AU

=> S (LEE, ?)/IN,AU  
'IN' IS NOT A VALID FIELD CODE  
'IN' IS NOT A VALID FIELD CODE  
L3 558398 (LEE, ?)/IN,AU

=> S L1 OR L2 OR L3  
L4 627388 L1 OR L2 OR L3

=> S L1 AND L2 AND L3  
L5 5 L1 AND L2 AND L3

=> DUPLICATE REMOVE L5  
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N  
PROCESSING COMPLETED FOR L5  
L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)

=> D IBIB AB L6 1,2

L6	ANSWER 1 OF 2	MEDLINE on STN	DUPLICATE 1
ACCESSION NUMBER:	2004474995	MEDLINE	
DOCUMENT NUMBER:	PubMed ID: 15386015		
TITLE:	Exogenous control of mammalian gene expression through modulation of RNA self-cleavage.		
COMMENT:	Comment in: Nature. 2004 Sep 23;431(7007):409. PubMed ID: 15385996		
AUTHOR:	Yen Laising; Svendsen Jennifer; <b>Lee Jeng-Shin</b> ; <b>Gray John T</b> ; Magnier Maxime; Baba Takashi; D'Amato Robert J; <b>Mulligan Richard C</b>		
CORPORATE SOURCE:	Department of Genetics, Harvard Institute of Human Genetics, Harvard Medical School, and Division of Molecular Medicine, Children's Hospital, Boston, Massachusetts 02115, USA.		
SOURCE:	Nature, (2004 Sep 23) 431 (7007) 471-6. Journal code: 0410462. ISSN: 1476-4687.		
PUB. COUNTRY:	England: United Kingdom		
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)		
LANGUAGE:	English		
FILE SEGMENT:	Priority Journals		

ENTRY MONTH: 200410  
ENTRY DATE: Entered STN: 20040924  
Last Updated on STN: 20041006  
Entered Medline: 20041005

AB Recent studies on the control of specific metabolic pathways in bacteria have documented the existence of entirely RNA-based mechanisms for controlling gene expression. These mechanisms involve the modulation of translation, transcription termination or RNA self-cleavage through the direct interaction of specific intracellular metabolites and RNA sequences. Here we show that an analogous RNA-based gene regulation system can effectively be designed for mammalian cells via the incorporation of sequences encoding self-cleaving RNA motifs into the transcriptional unit of a gene or vector. When correctly positioned, the sequences lead to potent inhibition of gene or vector expression, owing to the spontaneous cleavage of the RNA transcript. Administration of either oligonucleotides complementary to regions of the self-cleaving motif or a specific small molecule results in the efficient induction of gene expression, owing to inhibition of self-cleavage of the messenger RNA. Efficient regulation of transgene expression is shown in a variety of mammalian cell lines and live animals. In conjunction with other emerging technologies, this methodology may be particularly applicable to the development of gene regulation systems tailored to any small inducer molecule, and provide a novel means of biological sensing in vivo that may have an important application in the regulated delivery of protein therapeutics.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:575260 CAPLUS  
DOCUMENT NUMBER: 137:136065  
TITLE: Retroviral vectors containing SNV gag-pol capable of transducing therapeutic genes into quiescent cells and packaging cell lines for producing thereof  
INVENTOR(S): Summerford, Candace; **Gray, John T.**;  
**Lee, Jeng-Shin; Mulligan, Richard C.**  
PATENT ASSIGNEE(S): The Children's Medical Center Corporation, USA;  
President and Fellows of Harvard College  
SOURCE: PCT Int. Appl., 68 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059338	A2	20020801	WO 2002-US378	20020107
WO 2002059338	A3	20030724		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2433867	AA	20020801	CA 2002-2433867	20020107
EP 1358342	A2	20031105	EP 2002-714708	20020107
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRIORITY APPLN. INFO.:			US 2001-260199P	P 20010106
			WO 2002-US378	W 20020107

AB Methods of producing retroviral vector particles capable of transducing therapeutic genes into quiescent (non-dividing, resting) cells and methods of gene transfer to quiescent cells comprising infection with a retroviral particle described herein. The present invention is based on inventors' discoveries that retroviral vector particles, which encode the wild-type spleen necrosis virus (SNV) gag-pol gene products, can transfect quiescent cells and do not require a nuclear localization sequence (NLS) in the matrix protein to transfect quiescent cells. The invention relates to novel packaging cell lines useful for generating retroviral vector particles capable of infecting and transducing a DNA sequence of interest into quiescent cells, to construction of such cell lines and to methods of using the particles to introduce transgene into quiescent animal cells (particularly mammalian cells). Sequences required for packaging and reverse transcription can be derived from Moloney leukemia virus (MLV), SNV or other viruses. In particular embodiments, the heterologous envelope protein is the G glycoprotein of vesicular stomatitis virus (VSV G) or the amphotropic envelope of the MLV. The packaging cell lines and viral particles of the present invention can be used in gene therapy or gene replacement to introduce genes into a variety of quiescent cells.

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

L1 63641 S (GRAY, ?)/IN,AU  
L2 6393 S (MULLIGAN, ?)/IN,AU  
L3 558398 S (LEE, ?)/IN,AU  
L4 627388 S L1 OR L2 OR L3  
L5 5 S L1 AND L2 AND L3  
L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)

=> S L1 OR L2 OR L3

L7 627388 L1 OR L2 OR L3

=> S (KOTSOPOULOU, ?)/IN,AU

'IN' IS NOT A VALID FIELD CODE

'IN' IS NOT A VALID FIELD CODE

L8 42 (KOTSOPOULOU, ?)/IN,AU

=> S (KIM, ?)/IN,AU

'IN' IS NOT A VALID FIELD CODE

'IN' IS NOT A VALID FIELD CODE

L9 392484 (KIM, ?)/IN,AU

=> S (KINGSMAN, ?)/IN,AU

'IN' IS NOT A VALID FIELD CODE

'IN' IS NOT A VALID FIELD CODE

L10 744 (KINGSMAN, ?)/IN,AU

=> S (MITROPHANOUS, ?)/IN,AU

'IN' IS NOT A VALID FIELD CODE

'IN' IS NOT A VALID FIELD CODE

L11 137 (MITROPHANOUS, ?)/IN,AU

=> S L8 AND L9 AND L10 AND L11

L12 5 L8 AND L9 AND L10 AND L11

=> DUPLICATE REMOVE L12

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N

PROCESSING COMPLETED FOR L12



L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)

=> D IBIB AB L13 1,2

L13 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:781146 CAPLUS  
DOCUMENT NUMBER: 135:340191  
TITLE: HIV-1 and EIAV derived retroviral vector constructs  
with codon-optimized gag-pol genes and their uses  
INVENTOR(S): **Kingsman, Alan John; Kim, Narry;**  
**Kotsopoulou, Ekaterini;** Rohll, Jonathan;  
**Mitrophanous, Kyriacos Andreou**  
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Ltd., UK  
SOURCE: PCT Int. Appl., 201 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079518	A2	20011025	WO 2001-GB1784	20010418
WO 2001079518	A3	20020516		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2404129	AA	20011025	CA 2001-2404129	20010418
EP 1278878	A2	20030129	EP 2001-921651	20010418
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004508808	T2	20040325	JP 2001-577501	20010418
US 2005042234	A1	20050224	US 2003-258089	20030314
PRIORITY APPLN. INFO.:			GB 2000-9760	A 20000419
			WO 2001-GB1784	W 20010418

AB This invention claims a method of producing a replication defective retrovirus comprising transfecting a producer cell with the following: (i) a retroviral genome; (ii) a nucleotide sequence coding for retroviral gag and pol proteins; and (iii) nucleotide sequences encoding other essential viral packaging components not encoded by the nucleotide sequence of (ii); characterized in that the nucleotide sequence coding for retroviral gag and pol proteins is codon optimized for expression in the producer cell. The invention provides synthetic gag-pol polynucleotide sequences which will not be able to recombine or package viral mRNAs in infected cells. Codons in the region of the gag-pol gene which contains overlapping reading frames encoding gag and pol proteins are not optimized, to ensure efficient expression of the gag and pol proteins. The codon-optimized gag-pol sequences for HIV-1 and EIAV (equine infectious anemia virus) disrupt packaging signals near the 5' end of the gag-pol mRNA and also result in Rev/RRE-independent gag-pol mRNA expression and protein production. An example of the invention is an HIV-1 based vector system composed of three plasmids: one expressing codon-optimized gene gag-pol; one expressing VSV-G envelope proteins; and one expressing a 360-nucleotide "wild-type" gag sequence and a splice donor. RNA expression, protein expression, titers, and transduction efficiency of the system were determined. A similar vector system based on the non-primate lentivirus EIAV was constructed and characterized; however, sequences in the gag gene required

for packaging EIAV appear to differ from the HIV-1 packaging signal.

L13 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2000240070 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10775623  
TITLE: A Rev-independent human immunodeficiency virus type 1  
(HIV-1)-based vector that exploits a codon-optimized HIV-1  
gag-pol gene.  
AUTHOR: Kotsopoulou E; Kim V N; Kingsman A  
J; Kingsman S M; Mitrophanous K A  
CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of  
Biochemistry, University of Oxford, Oxford OX1 3QU, United  
Kingdom.  
SOURCE: Journal of virology, (2000 May) 74 (10) 4839-52.  
Journal code: 0113724. ISSN: 0022-538X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 200005  
ENTRY DATE: Entered STN: 20000518  
Last Updated on STN: 20000518  
Entered Medline: 20000511

AB The human immunodeficiency virus (HIV) genome is AU rich, and this imparts  
a codon bias that is quite different from the one used by human genes.  
The codon usage is particularly marked for the gag, pol, and env genes.  
Interestingly, the expression of these genes is dependent on the presence  
of the Rev/Rev-responsive element (RRE) regulatory system, even in  
contexts other than the HIV genome. The Rev dependency has been explained  
in part by the presence of RNA instability sequences residing in these  
coding regions. The requirement for Rev also places a limitation on the  
development of HIV-based vectors, because of the requirement to provide an  
accessory factor. We have now synthesized a complete codon-optimized  
HIV-1 gag-pol gene. We show that expression levels are high and that  
expression is Rev independent. This effect is due to an increase in the  
amount of gag-pol mRNA. Provision of the RRE in cis did not lower protein  
or RNA levels or stimulate a Rev response. Furthermore we have used this  
synthetic gag-pol gene to produce HIV vectors that now lack all of the  
accessory proteins. These vectors should now be safer than murine  
leukemia virus-based vectors.

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

L1 63641 S (GRAY, ?)/IN,AU  
L2 6393 S (MULLIGAN, ?)/IN,AU  
L3 558398 S (LEE, ?)/IN,AU  
L4 627388 S L1 OR L2 OR L3  
L5 5 S L1 AND L2 AND L3  
L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)  
L7 627388 S L1 OR L2 OR L3  
L8 42 S (KOTSOPOULOU, ?)/IN,AU  
L9 392484 S (KIM, ?)/IN,AU  
L10 744 S (KINGSMAN, ?)/IN,AU  
L11 137 S (MITROPHANOUS, ?)/IN,AU  
L12 5 S L8 AND L9 AND L10 AND L11  
L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)

=> S L8 OR L9 OR L10 OR L11

L14 393256 L8 OR L9 OR L10 OR L11

=> S L7 AND L14  
L15 108214 L7 AND L14

=> S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR RETROVIR? OR SIV  
OR MMV  
L16 646307 (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR  
RETROVIR? OR SIV OR MMV

=> S L16 AND L7  
L17 9889 L16 AND L7

=> S L16 AND L14  
L18 4794 L16 AND L14

=> S L16 AND L15  
L19 849 L16 AND L15

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

L1 63641 S (GRAY, ?)/IN,AU  
L2 6393 S (MULLIGAN, ?)/IN,AU  
L3 558398 S (LEE, ?)/IN,AU  
L4 627388 S L1 OR L2 OR L3  
L5 5 S L1 AND L2 AND L3  
L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)  
L7 627388 S L1 OR L2 OR L3  
L8 42 S (KOTSOPOULOU, ?)/IN,AU  
L9 392484 S (KIM, ?)/IN,AU  
L10 744 S (KINGSMAN, ?)/IN,AU  
L11 137 S (MITROPHANOUS, ?)/IN,AU  
L12 5 S L8 AND L9 AND L10 AND L11  
L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)  
L14 393256 S L8 OR L9 OR L10 OR L11  
L15 108214 S L7 AND L14  
L16 646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR  
L17 9889 S L16 AND L7  
L18 4794 S L16 AND L14  
L19 849 S L16 AND L15

=> S (CODON (S) OPTIMIZ?)  
L20 1201 (CODON (S) OPTIMIZ?)

=> S L16 AND L20  
L21 241 L16 AND L20

=> S L21 AND L7  
L22 5 L21 AND L7

=> DUPLICATE REMOVE L22  
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N  
PROCESSING COMPLETED FOR L22  
L23 2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)

=> D IBIB AB L23 1,2

L23 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2003125220 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12639249

TITLE: Characterization and selection of HIV-1 subtype C isolates for use in vaccine development.  
 AUTHOR: Williamson Carolyn; Morris Lynn; Maughan Maureen F; Ping Li-Hua; Dryga Sergey A; Thomas Robin; Reap Elizabeth A; Cilliers Tonie; van Harmelen Joanne; Pascual Alvaro; Ramjee Gita; **Gray Glenda**; Johnston Robert; Karim Salim Abdool; Swanstrom Ronald  
 CORPORATE SOURCE: Division of Medical Virology, University of Cape Town, Observatory, Cape Town, South Africa 7925..  
 cwilliam@curie.uct.ac.za  
 CONTRACT NUMBER: AI46023 (NIAID)  
 P30-AI50410 (NIAID)  
 SOURCE: AIDS research and human retroviruses, (2003 Feb) 19 (2) 133-44.  
 Journal code: 8709376. ISSN: 0889-2229.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; AIDS  
 OTHER SOURCE: GENBANK-AF543896; GENBANK-AF543897; GENBANK-AF543898; GENBANK-AF543899; GENBANK-AF543900; GENBANK-AF543901; GENBANK-AF543902; GENBANK-AF543903; GENBANK-AF543904; GENBANK-AF543905; GENBANK-AF543906; GENBANK-AF543907; GENBANK-AF543908; GENBANK-AF543909; GENBANK-AF543910; GENBANK-AF543911; GENBANK-AF543912; GENBANK-AF543913; GENBANK-AF543914; GENBANK-AF543915; GENBANK-AF543916; GENBANK-AF543917; GENBANK-AF543918; GENBANK-AF543919; GENBANK-AF543920; GENBANK-AF543921; GENBANK-AF543922; GENBANK-AF543923; GENBANK-AF543924; GENBANK-AF543925; GENBANK-AF543926; GENBANK-AF543927; GENBANK-AF543928; GENBANK-AF543929; GENBANK-AF543930; GENBANK-AF543931; GENBANK-AF543932; GENBANK-AF543933; GENBANK-AF543934; GENBANK-AF543935; GENBANK-AF543936; GENBANK-AF543937; GENBANK-AF543938; GENBANK-AF543939; GENBANK-AF543940; GENBANK-AF543941; GENBANK-AF543942; GENBANK-AF543943; GENBANK-AF543944; GENBANK-AF543945; GENBANK-AF543946; GENBANK-AF543947; GENBANK-AF543948; GENBANK-AF543949; GENBANK-AF543950; GENBANK-AF543951; GENBANK-AF543952; GENBANK-AF543953; GENBANK-AF543954; GENBANK-AF543955; GENBANK-AF543956; GENBANK-AF543957; GENBANK-AF543958; GENBANK-AF543959; GENBANK-AF543960; GENBANK-AF543961; GENBANK-AF543962; GENBANK-AF543963; GENBANK-AF543964; GENBANK-AF543965; GENBANK-AF543966; GENBANK-AF543967; GENBANK-AF543968; GENBANK-AF543969; GENBANK-AF543970; GENBANK-AF543971; GENBANK-AF543972; GENBANK-AF543973; GENBANK-AF543974; GENBANK-AF543975; GENBANK-AF543976; GENBANK-AF543977; GENBANK-AF543978; GENBANK-AF543979; GENBANK-AF543980; GENBANK-AF543981; GENBANK-AF543982; GENBANK-AF543983; GENBANK-AF543984; GENBANK-AF543985; GENBANK-AF543986; GENBANK-AF543987; GENBANK-AF543988; GENBANK-AF543989; GENBANK-AF543990; GENBANK-AF543991; GENBANK-AF543992; GENBANK-AF543993; GENBANK-AF543994; GENBANK-AF543995; GENBANK-AF543996; GENBANK-AF543997; GENBANK-AF543998; GENBANK-AF543999; GENBANK-AF544000; GENBANK-AF544001; GENBANK-AF544002; GENBANK-AF544003; GENBANK-AF544004; GENBANK-AF544005; GENBANK-AF544006; GENBANK-AF544007; GENBANK-AF544008; GENBANK-AF544009; GENBANK-AF544010  
 ENTRY MONTH: 200305  
 ENTRY DATE: Entered STN: 20030318  
 Last Updated on STN: 20030520  
 Entered Medline: 20030519  
 AB HIV-1 genetic diversity among circulating strains presents a



major challenge for **HIV-1** vaccine development, particularly for developing countries where less sequence information is available. To identify representative viruses for inclusion in candidate vaccines targeted for South Africa, we applied an efficient sequence survey strategy to samples from recently and chronically infected persons residing in potential vaccine trial sites. All 111 sequences were subtype C, including 30 partial gag, 26 partial pol, 27 V2-V3 env, and 28 V5-partial gp41 sequences. Of the 10 viruses cultured from recently infected individuals, 9 were R5 and 1 was R5X4. Two isolates, Du151 and Du422, collected within 2 months of infection, were selected as vaccine strains on the basis of their amino acid similarity to a derived South African consensus sequence. The selection of recently transmitted R5 isolates for vaccine design may provide an advantage in a subtype C R5-dominant epidemic. The full-length Du422 gag and Du151 pol and env genes were cloned into the Venezuelan equine encephalitis (VEE) replicon particle (VRP) expression system. Du422 Gag protein expressed from the VRP accumulated to a high level and was immunogenic as demonstrated by cytotoxic T lymphocyte responses in mice vaccinated with gag-VRPs. **Optimization of codon use for VRP expression in human cells did not enhance expression of the gag gene.** The cloned Du151 env gene encoded a functional protein as demonstrated by fusion of VRP-infected cells with cells expressing CD4 and CCR5. Genes identified in this study have been incorporated into the VEE VRP candidate vaccines targeted for clinical trial in South Africa.

L23 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:191238 CAPLUS

DOCUMENT NUMBER: 132:232375

TITLE: Packaging cell lines for generation of **retroviral** vector particles free of accessory proteins

INVENTOR(S): **Gray, John T.; Mulligan, Richard C.**

PATENT ASSIGNEE(S): The Children's Medical Center Corp., USA

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015819	A1	20000323	WO 1999-US20675	19990910
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9961396	A1	20000403	AU 1999-61396	19990910
PRIORITY APPLN. INFO.:			US 1998-100022P	P 19980911
			US 1998-100063P	P 19980912
			WO 1999-US20675	W 19990910

AB Novel packaging cell lines useful for generating viral accessory protein independent **HIV**-derived **retroviral** vector particles, methods of constructing such packaging cell lines and methods of using the viral accessory protein independent **HIV**-derived **retroviral** vector particles are disclosed. The cell lines carry the **retroviral** gag-pol and env genes with **codon** usage **optimized** for expression in the host cell and the nucleic acid to be packaged under the control of **retroviral** cis-acting sequences for packaging, reverse transcription, and integration. The gag-pol and env genes may be from different viruses and the gag and pol genes may be separated and from different viruses. Genes for accessory proteins and certain cis-acting elements (constitutive transport elements) are absent.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

L1 63641 S (GRAY, ?)/IN,AU  
 L2 6393 S (MULLIGAN, ?)/IN,AU  
 L3 558398 S (LEE, ?)/IN,AU  
 L4 627388 S L1 OR L2 OR L3  
 L5 5 S L1 AND L2 AND L3  
 L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)  
 L7 627388 S L1 OR L2 OR L3  
 L8 42 S (KOTSOPOULOU, ?)/IN,AU  
 L9 392484 S (KIM, ?)/IN,AU  
 L10 744 S (KINGSMAN, ?)/IN,AU  
 L11 137 S (MITROPHANOUS, ?)/IN,AU  
 L12 5 S L8 AND L9 AND L10 AND L11  
 L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)  
 L14 393256 S L8 OR L9 OR L10 OR L11  
 L15 108214 S L7 AND L14  
 L16 646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR  
 L17 9889 S L16 AND L7  
 L18 4794 S L16 AND L14  
 L19 849 S L16 AND L15  
 L20 1201 S (CODON (S) OPTIMIZ?)  
 L21 241 S L16 AND L20  
 L22 5 S L21 AND L7  
 L23 2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)

=> S L21 AND L14

L24 14 L21 AND L14

=> DUPLICATE REMOVE L24

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N

PROCESSING COMPLETED FOR L24

L25 8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)

=> D IBIB AB L25 1-8

L25 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:1078 CAPLUS

DOCUMENT NUMBER: 142:79860

TITLE: Use of **retroviral** vectors expressing  
 RARβ2 and/or an agonist thereof for neurite  
 regeneration in treating nerve injury

INVENTOR(S): Wong, Liang Fong; Mazarakis, Nicholas; **Kingsman,**  
**Alan**; McMahon, Stephen; Maden, Malcolm

PATENT ASSIGNEE(S): UK

SOURCE: U.S. Pat. Appl. Publ., 196 pp., Cont.-in-part of U.S.  
 Ser. No. 716,725.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 2004266715	A1	20041230	US 2004-838906	20040503

WO 2000057900	A2	20001005	WO 2000-GB1211	20000330
WO 2000057900	A3	20010215		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
WO 2001075135	A1	20011011	WO 2001-GB1478	20010330
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
WO 2002036170	A2	20020510	WO 2001-GB4866	20011102
WO 2002036170	A3	20020822		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003053991	A1	20030320	US 2002-239804	20020923
US 2004071675	A1	20040415	US 2003-429608	20030505
WO 2004031390	A1	20040415	WO 2003-GB4260	20031003
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004076613	A1	20040422	US 2003-716725	20031119
PRIORITY APPLN. INFO.:			GB 1999-7461	A 19990331
			WO 2000-GB1211	W 20000330
			GB 2000-24300	A 20001004
			GB 2000-26943	A 20001103
			GB 2001-2339	A 20010130
			WO 2001-GB1478	W 20010330
			GB 2001-22238	A 20010914
			WO 2001-GB4866	A2 20011102
			US 2002-937716	A2 20020701
			US 2002-239804	A2 20020923
			GB 2002-23076	A 20021004
			GB 2002-28314	A 20021204
			US 2003-429608	A2 20030505
			GB 2003-18213	A 20030804
			WO 2003-GB4260	A2 20031003
			US 2003-716725	A2 20031119

AB The present invention relates to the use of retinoic acid receptor

RAR- $\beta$ 2 and/or an agonist thereof in the preparation of a medicament to cause neurite development, neurite growth and/or neurite regeneration. The present invention is based on the finding that it is possible to cause neurite development, such as neurite outgrowth and/or neurite regeneration, by using RAR2 and/or an agonist thereof, and that RAR2 may be introduced into neuronal cells using **retroviral** vectors based on **lentiviral** vectors. In another aspect, the present invention relates to a method of treating a neurol. disorder such as a nerve injury comprising administering a pharmacol. active amount of an RAR2 receptor, and/or an agonist thereof, wherein said agonist is RA and/or CD2019. Provided sequence of plasmid vectors of invention.

L25 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:473147 CAPLUS

DOCUMENT NUMBER: 139:48169

TITLE: Packaging cells regulated by tetracycline-sodium butyrate system for producing high titer pseudotyped viral vectors, specifically equine infectious anemia virus vectors

INVENTOR(S): Olsen, John C.; **Mitrophanous, Kyriacos Andreou**; Rohll, Jonathan; **Kingsman, Alan John**; Ellard, Fiona Margaret

PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, USA

SOURCE: U.S. Pat. Appl. Publ., 98 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003113898	A1	20030619	US 2002-134643	20020430
CA 2344208	AA	20021030	CA 2001-2344208	20010430
PRIORITY APPLN. INFO.:			CA 2001-2344208	A 20010430
			US 2001-287048P	P 20010430

AB The present invention relates to methods for producing pseudotyped viral vectors with a broad host range which can be produced at sufficient titers in packaging and/or stable producer cell lines. Most specifically, the invention relates to the generation of pseudotyped **retroviral** vectors having vesicular stomatitis virus-G protein (VSV-G) as the membrane-associated viral envelope protein. The present invention describes a novel system for producing high titer vectors wherein the production of the vectors is activated by doxycycline, but only after an initial stimulus with sodium butyrate--full activation is not observed in the presence of doxycycline alone. However following an initial treatment with sodium butyrate, the system can be maintained in an active state by supplying doxycycline alone. The producer cell comprises: (i) a first nucleotide sequence (NS) encoding a toxic viral envelope protein operably linked to a promoter; wherein the promoter is operably linked to at least one copy of a TRE (tetracycline-responsive element); (ii) a second NS encoding a tetracycline modulator; (iii) a third NS encoding a **retrovirus** nucleocapsid protein; and (iv) a fourth NS comprising a **retroviral** sequence capable of being encapsidated in the nucleocapsid protein such that the **retroviral** vector particle titer obtainable from the producer cell is regulatable by tetracycline and an initial stimulus with sodium butyrate or functional analogs thereof. The present invention also relates to **lentiviral** vectors, in particular those derived from equine infectious anemia virus (EIAV), useful in gene delivery to non-dividing and dividing cells. Thus, our invention relates to a method for making a producer cell capable of making EIAV vector efficiently and safely and in an REV/RRE independent manner. The inventors found that woodchuck hepatitis virus (WHV) post-transcriptional regulatory element



(PRE) can substitute for the REV/RRE in the EIAV vector system.

L25 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2003202646 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12679787  
TITLE: Continuous high-titer **HIV-1** vector production.  
AUTHOR: Ikeda Yasuhiro; Takeuchi Yasuhiro; Martin Francisco; Cosset  
Francois-Loic; **Mitrophanous Kyriacos**; Collins  
Mary  
CORPORATE SOURCE: Department of Immunology and Molecular Pathology, Windeyer  
Institute, University College London, 46 Cleveland St.,  
London W1T 4JF, UK.  
SOURCE: Nature biotechnology, (2003 May) 21 (5) 569-72. Electronic  
Publication: 2003-04-07.  
Journal code: 9604648. ISSN: 1087-0156.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (EVALUATION STUDIES)  
Report; (TECHNICAL REPORT)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200401  
ENTRY DATE: Entered STN: 20030501  
Last Updated on STN: 20040106  
Entered Medline: 20040105

AB **Human immunodeficiency virus** type 1 (**HIV-1**)-based vectors are currently made by transient transfection,  
or using packaging cell lines in which expression of **HIV-1** Gag  
and Pol proteins is induced. Continuous vector production by cells in  
which **HIV-1** Gag-Pol is stably expressed would allow rapid and  
reproducible generation of large vector batches. However, attempts to  
make stable **HIV-1** packaging cells by transfection of plasmids  
encoding **HIV-1** Gag-Pol have resulted in cells which secrete only  
low levels of p24 antigen (20-80 ng/ml), possibly because of the  
cytotoxicity of **HIV-1** protease. Infection of cells with  
**HIV-1** can result in stable virus production; cell clones that  
produce up to 1,000 ng/ml secreted p24 antigen have been described. Here  
we report that expression of **HIV-1** Gag-Pol by a murine leukemia  
virus (MLV) vector allows constitutive, long-term, high-level (up to 850  
ng/ml p24) expression of **HIV-1** Gag. Stable packaging cells were  
constructed using **codon-optimized HIV-1**  
Gag-Pol and envelope proteins of gammaretroviruses; these producer cells  
could make up to 10(7) 293T infectious units (i.u.)/ml (20 293T  
i.u./cell/day) for at least three months in culture.

L25 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2002:276168 CAPLUS  
DOCUMENT NUMBER: 136:289952  
TITLE: **Retroviral** vector system comprising internal  
ribosome entry for Parkinson's disease gene therapy  
INVENTOR(S): **Kingsman, Alan John**; Mazarakis, Nicholas D.;  
Martin-Rendon, Enca; Azzouz, Mimoun; Rohll, Jonathan  
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK  
SOURCE: PCT Int. Appl., 106 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029065	A2	20020411	WO 2001-GB4433	20011005
WO 2002029065	A3	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2424738 AA 20020411 CA 2001-2424738 20011005  
AU 2001092093 A5 20020415 AU 2001-92093 20011005  
EP 1337655 A2 20030827 EP 2001-972317 20011005  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
JP 2004520016 T2 20040708 JP 2002-532634 20011005  
US 2004013648 A1 20040122 US 2003-408456 20030407  
US 2005002907 A1 20050106 US 2004-873573 20040621  
PRIORITY APPLN. INFO.: GB 2000-24550 A 20001006  
WO 2001-GB4433 W 20011005  
US 2003-408456 A2 20030407

AB The present invention relates to **retroviral** vector for treating  
a neurodegenerative disorder or Parkinson's disease. In particular the  
present invention relates to a **retroviral** vector lacking the rev  
responsive element and comprising two or more NOI (nucleotide sequence of  
interest) operably linked by one or more Internal Ribosome Entry Site(s).  
The said **lentiviral** vector comprise sequences encoding tyrosine  
hydroxylase, GTP-cyclohydrolase I or optionally aromatic amino acid Dopa  
decarboxylase. The invention also relates to transiently expression of  
NOI from bicistronic and tricistronic cassettes in heterologous human  
cells. EIAV-TRIC vectors uses for correcting the 6-hydroxydopamine  
(6-OHDA) and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) primate  
model of Parkinson's disease.

L25 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:781146 CAPLUS

DOCUMENT NUMBER: 135:340191

TITLE: **HIV-1 and EIAV derived retroviral**  
**vector constructs with codon-**  
**optimized gag-pol genes and their uses**  
INVENTOR(S): **Kingsman, Alan John; Kim, Narry;**  
**Kotsopoulou, Ekaterini; Rohll, Jonathan;**  
**Mitrophanous, Kyriacos Andreou**  
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Ltd., UK  
SOURCE: PCT Int. Appl., 201 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079518	A2	20011025	WO 2001-GB1784	20010418
WO 2001079518	A3	20020516		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

CA 2404129	AA	20011025	CA 2001-2404129	20010418
EP 1278878	A2	20030129	EP 2001-921651	20010418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508808	T2	20040325	JP 2001-577501	20010418
US 2005042234	A1	20050224	US 2003-258089	20030314
PRIORITY APPLN. INFO.:			GB 2000-9760	A 20000419
			WO 2001-GB1784	W 20010418

AB This invention claims a method of producing a replication defective **retrovirus** comprising transfecting a producer cell with the following: (i) a **retroviral** genome; (ii) a nucleotide sequence coding for **retroviral** gag and pol proteins; and (iii) nucleotide sequences encoding other essential viral packaging components not encoded by the nucleotide sequence of (ii); characterized in that the nucleotide sequence coding for **retroviral** gag and pol proteins is **codon optimized** for expression in the producer cell.

The invention provides synthetic gag-pol polynucleotide sequences which will not be able to recombine or package viral mRNAs in infected cells. Codons in the region of the gag-pol gene which contains overlapping reading frames encoding gag and pol proteins are not optimized, to ensure efficient expression of the gag and pol proteins. The **codon-optimized** gag-pol sequences for **HIV-1** and **EIAV** (equine infectious anemia virus) disrupt packaging signals near the 5' end of the gag-pol mRNA and also result in Rev/RRE-independent gag-pol mRNA expression and protein production. An example of the invention is an **HIV-1** based vector system composed of three plasmids: one expressing **codon-optimized** gene gag-pol; one expressing VSV-G envelope proteins; and one expressing a 360-nucleotide "wild-type" gag sequence and a splice donor. RNA expression, protein expression, titers, and transduction efficiency of the system were determined. A similar vector system based on the non-primate **lentivirus** **EIAV** was constructed and characterized; however, sequences in the gag gene required for packaging **EIAV** appear to differ from the **HIV-1** packaging signal.

L25 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:666894 CAPLUS  
DOCUMENT NUMBER: 133:262244  
TITLE: System for producing external guide sequence-encoding viral vectors for treatment of viral infections  
INVENTOR(S): Uden, Mark; **Mitrophanous, Kyriacos**  
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK  
SOURCE: PCT Int. Appl., 62 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055341	A1	20000921	WO 2000-GB1002	20000317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2363794	A1	20020109	GB 2001-22683	20000317
EP 1192265	A1	20020403	EP 2000-911067	20000317

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

JP 2002538829 T2 20021119 JP 2000-605758 20000317  
US 6783981 B1 20040831 US 2001-936572 20011211

PRIORITY APPLN. INFO.: GB 1999-6177 A 19990317  
WO 2000-GB1002 W 20000317

AB A viral vector production system is provided which system comprises: (i) a viral genome comprising at least one first nucleotide sequence encoding a gene product capable of binding to and effecting the cleavage, directly or indirectly, of a second nucleotide sequence, or transcription product thereof, encoding a viral polypeptide required for the assembly of viral particles; (ii) a third nucleotide sequence encoding said viral polypeptide required for the assembly of the viral genome into viral particles, which third nucleotide sequence has a different nucleotide sequence to the second nucleotide sequence such that said third nucleotide sequence, or transcription product thereof, is resistant to cleavage directed by said gene product; wherein at least one of the gene products is an external guide sequence (EGS) capable of binding to and effecting the cleavage by RNase P of the second nucleotide sequence. The viral vector production system may be used to produce viral particles for use in treating or preventing viral infection. Thus, a system for producing HIV particles encoding EGSs (and, optionally, anti-HIV ribozymes or antisense RNAs) includes an HIV genome encoding the EGS and nucleotide constructs encoding the components required for packaging the viral genome in the producer cell. In contrast to the prior art, although the packaging components have substantially the same amino acid sequence as the corresponding components of the target virus, the inhibitory RNA mols. do not affect production of the viral particles in the producer cells because the nucleotide sequence of the packaging components used in the viral system have been modified to prevent the inhibitory RNA mols. from effecting cleavage or degradation of the RNA transcripts produced from the constructs.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2000240070 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10775623  
TITLE: A Rev-independent **human immunodeficiency virus** type 1 (HIV-1)-based vector that exploits a **codon-optimized HIV** -1 gag-pol gene.  
AUTHOR: Kotsopoulou E; Kim V N; Kingsman A J; Kingsman S M; Mitrophanous K A  
CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom.  
SOURCE: Journal of virology, (2000 May) 74 (10) 4839-52.  
Journal code: 0113724. ISSN: 0022-538X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 200005  
ENTRY DATE: Entered STN: 20000518  
Last Updated on STN: 20000518  
Entered Medline: 20000511

AB The **human immunodeficiency virus** (HIV) genome is AU rich, and this imparts a codon bias that is quite different from the one used by **human** genes. The codon usage is particularly marked for the gag, pol, and env genes. Interestingly, the expression of these genes is dependent on the presence of the Rev/Rev-responsive element (RRE) regulatory system, even in



contexts other than the **HIV** genome. The Rev dependency has been explained in part by the presence of RNA instability sequences residing in these coding regions. The requirement for Rev also places a limitation on the development of **HIV**-based vectors, because of the requirement to provide an accessory factor. We have now synthesized a complete **codon-optimized HIV-1 gag-pol** gene. We show that expression levels are high and that expression is Rev independent. This effect is due to an increase in the amount of gag-pol mRNA. Provision of the RRE in cis did not lower protein or RNA levels or stimulate a Rev response. Furthermore we have used this synthetic gag-pol gene to produce **HIV** vectors that now lack all of the accessory proteins. These vectors should now be safer than murine leukemia virus-based vectors.

L25 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 ACCESSION NUMBER: 2000:431853 BIOSIS  
 DOCUMENT NUMBER: PREV200000431853  
 TITLE: Characterization of the equine infectious anaemia virus S2 protein.  
 AUTHOR(S): Yoon, Soonsang; **Kingsman, Susan M.**;  
**Kingsman, Alan J.**; Wilson, Stuart A.;  
**Mitrophanous, Kyriacos A.** [Reprint author]  
 CORPORATE SOURCE: Oxford Biomedica (UK) Ltd, Oxford Science Park, Oxford, OX4 4GA, UK  
 SOURCE: Journal of General Virology, (September, 2000) Vol. 81, No. 9, pp. 2189-2194. print.  
 CODEN: JGVIAY. ISSN: 0022-1317.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 11 Oct 2000  
 Last Updated on STN: 10 Jan 2002

AB S2 is an accessory protein of equine infectious anaemia virus (EIAV), the function of which is unknown. In order to gain insight into the function of S2, the intracellular localization of the protein, its interaction with viral proteins and its incorporation into viral particles have been investigated. Immunolocalization of S2 revealed punctuate staining in the cytoplasm and the S2 protein coprecipitated with the EIAV Gag precursor. Despite overexpression of S2 through the use of a **codon-optimized** sequence, there was no preferential association of S2 with EIAV particles. These data suggest that S2 may function to organize the Gag protein during particle assembly in the cytoplasm but that it is unlikely to be involved in the early stages of the virus life-cycle.

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

L1 63641 S (GRAY, ?)/IN,AU  
 L2 6393 S (MULLIGAN, ?)/IN,AU  
 L3 558398 S (LEE, ?)/IN,AU  
 L4 627388 S L1 OR L2 OR L3  
 L5 5 S L1 AND L2 AND L3  
 L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)  
 L7 627388 S L1 OR L2 OR L3  
 L8 42 S (KOTSOPLOULOU, ?)/IN,AU  
 L9 392484 S (KIM, ?)/IN,AU  
 L10 744 S (KINGSMAN, ?)/IN,AU  
 L11 137 S (MITROPHANOUS, ?)/IN,AU  
 L12 5 S L8 AND L9 AND L10 AND L11  
 L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)  
 L14 393256 S L8 OR L9 OR L10 OR L11

L15 108214 S L7 AND L14  
 L16 646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR  
 L17 9889 S L16 AND L7  
 L18 4794 S L16 AND L14  
 L19 849 S L16 AND L15  
 L20 1201 S (CODON (S) OPTIMIZ?)  
 L21 241 S L16 AND L20  
 L22 5 S L21 AND L7  
 L23 2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)  
 L24 14 S L21 AND L14  
 L25 8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)

=> S (GAGPOL OR GAG OR POL)  
 L26 65288 (GAGPOL OR GAG OR POL)

=> S L26 AND L20  
 L27 142 L26 AND L20

=> S L27 AND (L7 OR L14)  
 L28 20 L27 AND (L7 OR L14)

=> S L28 NOT (L22 OR L24)  
 L29 2 L28 NOT (L22 OR L24)

=> DUPLICATE REMOVE L29  
 DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS'  
 KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N  
 PROCESSING COMPLETED FOR L29  
 L30 1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)

=> D IBIB AB L30

L30. ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1  
 ACCESSION NUMBER: 2001021699 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10950976  
 TITLE: Characterization of the equine infectious anaemia virus S2 protein.  
 AUTHOR: Yoon S; **Kingsman S M; Kingsman A J;**  
 Wilson S A; **Mitrophanous K A**  
 CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, UK.  
 SOURCE: Journal of general virology, (2000 Sep) 81 (Pt 9) 2189-94. Journal code: 0077340. ISSN: 0022-1317.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200011  
 ENTRY DATE: Entered STN: 20010322  
 Last Updated on STN: 20020212  
 Entered Medline: 20001109  
 AB S2 is an accessory protein of equine infectious anaemia virus (EIAV), the function of which is unknown. In order to gain insight into the function of S2, the intracellular localization of the protein, its interaction with viral proteins and its incorporation into viral particles have been investigated. Immunolocalization of S2 revealed punctate staining in the cytoplasm and the S2 protein co-precipitated with the EIAV **Gag** precursor. Despite overexpression of S2 through the use of a **codon-optimized** sequence, there was no preferential association of S2 with EIAV particles. These data suggest that S2 may function to organize the **Gag** protein during particle assembly in the cytoplasm but that it is unlikely to be involved in the early stages

of the virus life-cycle.

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

```
L1      63641 S (GRAY, ?)/IN,AU
L2      6393 S (MULLIGAN, ?)/IN,AU
L3      558398 S (LEE, ?)/IN,AU
L4      627388 S L1 OR L2 OR L3
L5      5 S L1 AND L2 AND L3
L6      2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7      627388 S L1 OR L2 OR L3
L8      42 S (KOTSOPOULOU, ?)/IN,AU
L9      392484 S (KIM, ?)/IN,AU
L10     744 S (KINGSMAN, ?)/IN,AU
L11     137 S (MITROPHANOUS, ?)/IN,AU
L12     5 S L8 AND L9 AND L10 AND L11
L13     2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14     393256 S L8 OR L9 OR L10 OR L11
L15     108214 S L7 AND L14
L16     646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17     9889 S L16 AND L7
L18     4794 S L16 AND L14
L19     849 S L16 AND L15
L20     1201 S (CODON (S) OPTIMIZ?)
L21     241 S L16 AND L20
L22     5 S L21 AND L7
L23     2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24     14 S L21 AND L14
L25     8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26     65288 S (GAGPOL OR GAG OR POL)
L27     142 S L26 AND L20
L28     20 S L27 AND (L7 OR L14)
L29     2 S L28 NOT (L22 OR L24)
L30     1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)
```

=> S (LACK? OR DEVOID? OR DEFICIENT? OR "without")

L31 4339034 (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")

=> s ("CTE" or "CTEs" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))

L32 2584 ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))

=> S ("RRE" or "REV" or (rev (s) response (s) element?))

UNMATCHED LEFT PARENTHESIS '("RRE"'

The number of right parentheses in a query must be equal to the number of left parentheses.

=> S ("RRE" or "REV" or (rev (s) response (s) element?))

L33 34022 ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))

=> s ("CTE" or "CTEs" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))

L34 2598 ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))

=> d his

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

```
L1      63641 S (GRAY, ?)/IN,AU
L2      6393 S (MULLIGAN, ?)/IN,AU
```

L3 558398 S (LEE, ?)/IN,AU  
 L4 627388 S L1 OR L2 OR L3  
 L5 5 S L1 AND L2 AND L3  
 L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)  
 L7 627388 S L1 OR L2 OR L3  
 L8 42 S (KOTSOPOULOU, ?)/IN,AU  
 L9 392484 S (KIM, ?)/IN,AU  
 L10 744 S (KINGSMAN, ?)/IN,AU  
 L11 137 S (MITROPHANOUS, ?)/IN,AU  
 L12 5 S L8 AND L9 AND L10 AND L11  
 L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)  
 L14 393256 S L8 OR L9 OR L10 OR L11  
 L15 108214 S L7 AND L14  
 L16 646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR  
 L17 9889 S L16 AND L7  
 L18 4794 S L16 AND L14  
 L19 849 S L16 AND L15  
 L20 1201 S (CODON (S) OPTIMIZ?)  
 L21 241 S L16 AND L20  
 L22 5 S L21 AND L7  
 L23 2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)  
 L24 14 S L21 AND L14  
 L25 8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)  
 L26 65288 S (GAGPOL OR GAG OR POL)  
 L27 142 S L26 AND L20  
 L28 20 S L27 AND (L7 OR L14)  
 L29 2 S L28 NOT (L22 OR L24)  
 L30 1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)  
 L31 4339034 S (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")  
 L32 2584 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))  
 L33 34022 S ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))  
 L34 2598 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))

=> s l33 or l34

L35 36410 L33 OR L34

=> s l31 (s) l35

L36 870 L31 (S) L35

=> s l36 and l16

L37 428 L36 AND L16

=> s l37 and l20

L38 5 L37 AND L20

=> duplicate remove l38

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L38

L39 2 DUPLICATE REMOVE L38 (3 DUPLICATES REMOVED)

=> d ibib ab l39 1,2

L39 ANSWER 1 OF 2

MEDLINE on STN

DUPLICATE 1

ACCESSION NUMBER: 2003456252 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14517067

TITLE: Novel engineered HIV-1 East African Clade-A gp160  
 plasmid construct induces strong humoral and cell-mediated  
 immune responses in vivo.

AUTHOR: Muthumani Karuppiah; Zhang Donghui; Dayes Nathanael S;  
 Hwang Daniel S; Calarota Sandra A; Choo Andrew Y; Boyer  
 Jean D; Weiner David B

CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University



SOURCE: of Pennsylvania, Philadelphia, PA 19104, USA.  
 Virology, (2003 Sep 15) 314 (1) 134-46.  
 Journal code: 0110674. ISSN: 0042-6822.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200311  
 ENTRY DATE: Entered STN: 20031001  
 Last Updated on STN: 20031104  
 Entered Medline: 20031103

AB **HIV-1** sequences are highly diverse due to the inaccuracy of the viral reverse transcriptase. This diversity has been studied and used to categorize **HIV** isolates into subtypes or clades, which are geographically distinct. To develop effective vaccines against **HIV-1**, immunogens representing different subtypes may be important for induction of cross-protective immunity, but little data exist describing and comparing the immunogenicity induced by different subtype-based vaccines. This issue is further complicated by poor expression of **HIV** structural antigens due to rev dependence. One costly approach is to **codon optimize** each subtype construct to be examined. Interestingly, cis-acting transcriptional elements (CTE) can also by pass rev restriction by a rev independent export pathway. We reasoned that rev+CTE constructs might have advantages for such expression studies. A subtype A envelope sequence from a viral isolate from east Africa was cloned into a eukaryotic expression vector under the control of the CMV-IE promoter. The utility of inclusion of the Mason-Pfizer monkey virus (MPV)-**CTE** with/**without** **rev** for driving envelope expression and immunogenicity was examined. Expression of envelope (gp120) was confirmed by immunoblot analysis and by pseudotype virus infectivity assays. The presence of rev and the CTE together increased envelope expression and viral infection. Furthermore the CTE+rev construct was significantly more immunogenic then CTE alone vector. Isotype analysis and cytokine profiles showed strong Th1 response in plasmid-immunized mice, which also demonstrated the superior nature of the rev+CTE construct. These responses were of similar or greater magnitude to a **codon-optimized** construct. The resulting cellular immune responses were highly cross-reactive with a **HIV-1** envelope subtype B antigen. This study suggests a simple strategy for improving the expression and immunogenicity of **HIV** subtype-specific envelope antigens as plasmid or vector-borne immunogens.

L39 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:276168 CAPLUS  
 DOCUMENT NUMBER: 136:289952  
 TITLE: **Retroviral** vector system comprising internal ribosome entry for Parkinson's disease gene therapy  
 INVENTOR(S): Kingsman, Alan John; Mazarakis, Nicholas D.; Martin-Rendon, Enca; Azzouz, Mimoun; Rohll, Jonathan  
 PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK  
 SOURCE: PCT Int. Appl., 106 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029065	A2	20020411	WO 2001-GB4433	20011005
WO 2002029065	A3	20021227		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,			

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,  
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
 US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2424738	AA	20020411	CA 2001-2424738	20011005
AU 2001092093	A5	20020415	AU 2001-92093	20011005
EP 1337655	A2	20030827	EP 2001-972317	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004520016	T2	20040708	JP 2002-532634	20011005
US 2004013648	A1	20040122	US 2003-408456	20030407
US 2005002907	A1	20050106	US 2004-873573	20040621
PRIORITY APPLN. INFO.:			GB 2000-24550	A 20001006
			WO 2001-GB4433	W 20011005
			US 2003-408456	A2 20030407

AB The present invention relates to **retroviral** vector for treating a neurodegenerative disorder or Parkinson's disease. In particular the present invention relates to a **retroviral** vector **lacking** the **rev** responsive element and comprising two or more NOI (nucleotide sequence of interest) operably linked by one or more Internal Ribosome Entry Site(s). The said **lentiviral** vector comprise sequences encoding tyrosine hydroxylase, GTP-cyclohydrolase I or optionally aromatic amino acid Dopa decarboxylase. The invention also relates to transiently expression of NOI from bicistronic and tricistronic cassettes in heterologous human cells. EIAV-TRIC vectors uses for correcting the 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) primate model of Parkinson's disease.

=> d his

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

L1	63641 S (GRAY, ?)/IN,AU
L2	6393 S (MULLIGAN, ?)/IN,AU
L3	558398 S (LEE, ?)/IN,AU
L4	627388 S L1 OR L2 OR L3
L5	5 S L1 AND L2 AND L3
L6	2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7	627388 S L1 OR L2 OR L3
L8	42 S (KOTSOPOULOU, ?)/IN,AU
L9	392484 S (KIM, ?)/IN,AU
L10	744 S (KINGSMAN, ?)/IN,AU
L11	137 S (MITROPHANOUS, ?)/IN,AU
L12	5 S L8 AND L9 AND L10 AND L11
L13	2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14	393256 S L8 OR L9 OR L10 OR L11
L15	108214 S L7 AND L14
L16	646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17	9889 S L16 AND L7
L18	4794 S L16 AND L14
L19	849 S L16 AND L15
L20	1201 S (CODON (S) OPTIMIZ?)
L21	241 S L16 AND L20
L22	5 S L21 AND L7
L23	2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24	14 S L21 AND L14
L25	8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26	65288 S (GAGPOL OR GAG OR POL)

L27 142 S L26 AND L20  
 L28 20 S L27 AND (L7 OR L14)  
 L29 2 S L28 NOT (L22 OR L24)  
 L30 1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)  
 L31 4339034 S (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")  
 L32 2584 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))  
 L33 34022 S ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))  
 L34 2598 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))  
 L35 36410 S L33 OR L34  
 L36 870 S L31 (S) L35  
 L37 428 S L36 AND L16  
 L38 5 S L37 AND L20  
 L39 2 DUPLICATE REMOVE L38 (3 DUPLICATES REMOVED)

=> s all (s) accessory (s) (factors or proteins or polypeptides)  
 L40 171 ALL (S) ACCESSORY (S) (FACTORS OR PROTEINS OR POLYPEPTIDES)

=> s l40 (s) l31  
 L41 11 L40 (S) L31

=> s l41 and l16  
 L42 9 L41 AND L16

=> duplicate remove l42  
 DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'  
 KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
 PROCESSING COMPLETED FOR L42  
 L43 3 DUPLICATE REMOVE L42 (6 DUPLICATES REMOVED)

=> d ibib ab l43 1,2,3

L43 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1  
 ACCESSION NUMBER: 2003353367 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 12885348  
 TITLE: **Lentivirus**-mediated gene transfer and expression  
 in established human tumor antigen-specific cytotoxic T  
 cells and primary unstimulated T cells.  
 AUTHOR: Zhou Xianzheng; Cui Yan; Huang Xin; Yu Zhiwei; Thomas Amy  
 M; Ye Zhaohui; Pardoll Drew M; Jaffee Elizabeth M; Cheng  
 Linzhao  
 CORPORATE SOURCE: Division of Immunology and Hematopoiesis, The Sidney Kimmel  
 Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins  
 University School of Medicine, Baltimore, MD 21231, USA..  
 zhoux058@umh.edu  
 SOURCE: Human gene therapy, (2003 Jul 20) 14 (11) 1089-105.  
 Journal code: 9008950. ISSN: 1043-0342.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200309  
 ENTRY DATE: Entered STN: 20030730  
 Last Updated on STN: 20030928  
 Entered Medline: 20030926  
 AB In this report, we evaluated the efficiency of stable gene transfer into  
 established CD8(+) human tumor antigen-specific cytotoxic T cell (CTL)  
 lines and peripheral blood lymphocytes (PBL) by oncoretroviral and  
**lentiviral** vectors. In the oncoretroviral vector, the green  
 fluorescent protein (GFP) reporter gene was regulated by the murine stem  
 cell virus (MSCV) promoter. In three **human**  
**immunodeficiency virus** type 1 (HIV-1)-based  
**lentiviral** vectors, the GFP transgene was regulated by either a  
 chimeric MSCV/HIV-1 promoter, or cellular promoters from

human housekeeping genes PGK and EF1 alpha. We found that several lines of proliferating tumor-specific CTL were poorly (=2%) transduced by the oncoretroviral vector that transduced Jurkat T cell line efficiently (=80%). In contrast, three **lentiviral** vectors transduced 38-63% of these proliferating CTL. More interestingly, all **lentiviral** vectors packaged without the HIV-1 accessory proteins transduced human bulk PBL and purified CD4(+) and CD8(+) lymphocyte subsets without prior stimulation. Detailed analysis indicated that the **lentiviral** vectors containing the EF1 alpha or PGK ubiquitous promoter can transduce unstimulated PBL and achieve low-level transgene expression in the absence of any T-cell activation. However, T-cell activation subsequent to the transduction of unstimulated PBL is required for high-level transgene expression. Transduced PBL expressing transgene delivered by the **lentiviral** vectors still preserved resting and naive cell phenotypes. Taken together, prior T cell stimulation and HIV-1 accessory proteins are dispensable for **lentivirus**-mediated gene transfer into resting naive and memory T lymphocytes. These results will have significant implications for the study of T-cell biology and for the improvement of clinical gene therapies of acquired immune deficiency syndrome (AIDS) and cancer.

L43 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 ACCESSION NUMBER: 2004:165713 BIOSIS  
 DOCUMENT NUMBER: PREV200400161037  
 TITLE: **Lentiviral** transfert of a dominant negative mutant of FADD in CD34+ hematopoietic progenitors from myelodysplastic syndromes normalizes BFU-E growth and inhibits apoptosis of erythroid differentiated cells.  
 AUTHOR(S): Claessens, Yann-Erick [Reprint Author]; Dubart-Kupperschmitt, Anne [Reprint Author]; Park, Sophie V. [Reprint Author]; Mariot, Virginie [Reprint Author]; Picard, Francoise; Chretien, Stany [Reprint Author]; Dreyfus, Francois [Reprint Author]; Lacombe, Catherine [Reprint Author]; Mayeux, Patrick [Reprint Author]; Fontenay, Michaela [Reprint Author]  
 CORPORATE SOURCE: Department of Hematology, Cochin Institute, INSERM U567, Paris, France  
 SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 912a. print.  
 Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.  
 CODEN: BLOOAW. ISSN: 0006-4971.  
 DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 Conference; (Meeting Poster)  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 24 Mar 2004  
 Last Updated on STN: 24 Mar 2004  
 AB Introduction: Ineffective erythropoiesis of myelodysplastic syndromes (MDS) is partly due to excessive apoptosis of differentiated erythroid cells. We have previously demonstrated that both the death domain receptor Fas and its ligand are overexpressed and that blocking their interaction with the Fas:Fc chimera inhibits apoptosis. In this work, we used the **lentiviral** transfert of a dominant negative form of the Fas-associated death domain (FADD) coding sequence to investigate the role of Fas-mediated signaling in normal and MDS erythropoiesis. Materials and methods: ATG-AU1-FADDdn construct was inserted into the HIV-derived **lentiviral** vector TRIPDELTAU3 containing a sequence encoding the EGFP, at the BamHI-XhoI cloning sites downstream the EF1alpha promoter. TRIPDELTAU3-EF1alpha/FADDwt and TRIPDELTAU3-EF1alpha/EGFP vectors were used as controls. CD34+ cells isolated from normal (n=5) and

MDS (n=10) marrows were infected for 2 days with vector particles produced by co-transfections of 293T cells by the TRIP vectors and an encapsidation plasmid **lacking all accessory HIV-1 proteins**. Then, cells were maintained in culture conditions allowing the erythroid differentiation. Cell counting, cytological analysis and immunophenotyping were performed every three days. Transduction efficiency and apoptosis were measured by the percentage of EGFP and annexin V positive cells, respectively. Immature erythroid progenitors ie BFU-E were quantified at day 7 of the liquid culture in clonogenic assays. Results: As expected Fas expression was increased in MDS cultures compared to normal ones. At day 7, mean percentages of EGFP(+) cells were 57.4+-10.9% and 50.8+-16.3% in TRIPDELTAU3-EF1alpha/FADDdn-transduced MDS (MDS FADDdn) and normal cultures, respectively. BFU-Es' number was significantly increased in MDS FADDdn cells compared to MDS EGFP cells (p=0.047) and normalized compared to controls although it was decreased in MDS FADDwt treated cells compared to MDS EGFP cells (p=0.011). At day 14, the mean percentage of apoptotic cells significantly decreased from 36.2+-13.6% in MDS EGFP to 16.5+-6.5% in MDS FADDdn (p=0.0046). The rate of apoptosis was not modified in normal controls. Furthermore, MDS FADDdn cells were resistant to Fas-dependent induction of apoptosis by the Fas agonist CH11. However, the kinetic of erythroid differentiation in MDS FADDdn cultures remained similar to MDS EGFP and normal cultures. Finally, transduction of MDS cells with TRIPDELTAU3-EF1alpha/FADDwt resulted in a dramatic decrease of the percentages of EGFP(+) or Fas(+) cells suggesting that non transduced and Fas(-) cells were positively selected. Conclusion: These data established the crucial role of Fas-dependent signaling in the abnormal apoptosis of MDS erythroid lineage.

L43 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2  
 ACCESSION NUMBER: 2000240070 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10775623  
 TITLE: A Rev-independent **human immunodeficiency virus** type 1 (HIV-1)-based vector that exploits a codon-optimized HIV-1 gag-pol gene.  
 AUTHOR: Kotsopoulou E; Kim V N; Kingsman A J; Kingsman S M; Mitrophanous K A  
 CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom.  
 SOURCE: Journal of virology, (2000 May) 74 (10) 4839-52.  
 Journal code: 0113724. ISSN: 0022-538X.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; AIDS  
 ENTRY MONTH: 200005  
 ENTRY DATE: Entered STN: 20000518  
 Last Updated on STN: 20000518  
 Entered Medline: 20000511

AB The **human immunodeficiency virus** (HIV) genome is AU rich, and this imparts a codon bias that is quite different from the one used by **human** genes. The codon usage is particularly marked for the gag, pol, and env genes. Interestingly, the expression of these genes is dependent on the presence of the Rev/Rev-responsive element (RRE) regulatory system, even in contexts other than the HIV genome. The Rev dependency has been explained in part by the presence of RNA instability sequences residing in these coding regions. The requirement for Rev also places a limitation on the development of HIV-based vectors, because of the requirement to provide an accessory factor. We have now synthesized a complete codon-optimized HIV-1 gag-pol gene. We show that expression levels are high and that expression is Rev independent. This effect is



due to an increase in the amount of gag-pol mRNA. Provision of the RRE in cis did not lower protein or RNA levels or stimulate a Rev response. Furthermore we have used this synthetic gag-pol gene to produce HIV vectors that now **lack all** of the **accessory proteins**. These vectors should now be safer than murine leukemia virus-based vectors.

=> d his

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

```

L1      63641 S (GRAY, ?)/IN,AU
L2      6393 S (MULLIGAN, ?)/IN,AU
L3      558398 S (LEE, ?)/IN,AU
L4      627388 S L1 OR L2 OR L3
L5      5 S L1 AND L2 AND L3
L6      2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7      627388 S L1 OR L2 OR L3
L8      42 S (KOTSOPOULOU, ?)/IN,AU
L9      392484 S (KIM, ?)/IN,AU
L10     744 S (KINGSMAN, ?)/IN,AU
L11     137 S (MITROPHANOUS, ?)/IN,AU
L12     5 S L8 AND L9 AND L10 AND L11
L13     2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14     393256 S L8 OR L9 OR L10 OR L11
L15     108214 S L7 AND L14
L16     646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17     9889 S L16 AND L7
L18     4794 S L16 AND L14
L19     849 S L16 AND L15
L20     1201 S (CODON (S) OPTIMIZ?)
L21     241 S L16 AND L20
L22     5 S L21 AND L7
L23     2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24     14 S L21 AND L14
L25     8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26     65288 S (GAGPOL OR GAG OR POL)
L27     142 S L26 AND L20
L28     20 S L27 AND (L7 OR L14)
L29     2 S L28 NOT (L22 OR L24)
L30     1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)
L31     4339034 S (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")
L32     2584 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))
L33     34022 S ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))
L34     2598 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))
L35     36410 S L33 OR L34
L36     870 S L31 (S) L35
L37     428 S L36 AND L16
L38     5 S L37 AND L20
L39     2 DUPLICATE REMOVE L38 (3 DUPLICATES REMOVED)
L40     171 S ALL (S) ACCESSORY (S) (FACTORS OR PROTEINS OR POLYPEPTIDES)
L41     11 S L40 (S) L31
L42     9 S L41 AND L16
L43     3 DUPLICATE REMOVE L42 (6 DUPLICATES REMOVED)

```

Day : Thursday  
Date: 4/21/2005

Time: 17:03:21

**PALM INTRANET**

## Inventor Information for 09/393795

Inventor Name	City	State/Country
GRAY, JOHN T.	WEST ROXBURY	MASSACHUSETTS
MULLIGAN, RICHARD	LINCOLN	MASSACHUSETTS
SHIN LEE, JENG	LINCOLN	MASSACHUSETTS

[Appln Info](#)[Contents](#)[Petition Info](#)[Atty/Agent Info](#)[Continuity Data](#)[Foreign Data](#)

Search Another: Application#

or Patent#

PCT /  /

or PG PUBS #

Attorney Docket #

Bar Code #

To go back use Back button on your browser toolbar.

Back to [PALM](#) | [ASSIGNMENT](#) | [OASIS](#) | [Home page](#)